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Pesticide Fact Sheet Number 35: CAPTAFOL

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16. Abstract (Limit: 200 words)

This document contains up-to-date chemical information, including a summary of the Agency's regulatory position and rationale, on a specific pesticide or group of pesticides. A Fact Sheet is issued after one of the following actions has occurred.

1. Issuance or reissuance of a registration standard,
2. Issuance of each special review document,
3. Registration of a significantly changed use pattern,
4. Registration of a new chemical, or
5. An immediate need for information to resolve controversial issues relating to a specific chemical or use pattern.

17. Document Analysis a. Descriptors

Pesticides, regulations, Chemical Information Fact Sheet, Use Patterns, Science Findings

b. Identifiers/Open-Ended Terms

c. COSATI Field/Group

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Washington, DC 20460

EPA

Pesticide Fact Sheet

Name of Chemical: CAPTAFOL
Reason for Issuance:
Date Issued: October 1, 1984
Fact Sheet Number: 35

1. Description of Chemical

Generic Name: cis-N-[(1,1,2,2-tetrachloroethyl) thio]-4-cyclohexene-1,2-dicarboximide

Common Name: Captafol

Trade Names: Difolatan, Folcid, Haipen, Merpafol, Ortho 5865, Sanspor and Sulfemmide

EPA Shaughnessy Code: 081701
Chemical Abstract Service (CAS) Number: 2425-06-1
Year of Initial Registration: May 21, 1962
Pesticide Type: Fungicide
Chemical Family: Phthalimide
U.S. Producer: Chevron Chemical Company

2. Use Patterns and Formulations

Application Sites: Apples (Midwestern and Eastern states only), apricots, blueberries, cherries (unspecified-use in California and Oregon only), cherries (sour), cranberries, grapefruit, lemons, limes (Florida only), macadamia nuts (Hawaii), nectarines, oranges (Florida only), peaches, pineapples, plums, prunes, tangerines, corn (sweet, Florida only), cucumbers, melons, onions, potatoes, taro (wetland) (Hawaii only), tomatoes (mechanically harvested only), watermelons, peanuts, seed treatment uses [corn (field), cotton, peanuts, rice and sorghum (grain and forage)] and wood.

Types of Formulations: Dusts, emulsifiable concentrates, flowable suspensions, wettable powders, and water dispersible granules.

Types and Methods of Application: Dusting, spraying, misting, and dipping under pressure for wood treatment.

Application Rates: See use patterns in USDA Compilations of Registered Uses of Fungicides and Nematicides, Part I, Pages C-09-95.01 through C-09-95.11.

Usual Carriers: Clay, talc, silica, water.

3. Scientific Findings

Chemical Characteristics:

Physical State: Crystalline solid
Color: White

Odor: Slight characteristic pungent odor
Melting Point: Range 156-161°C (162°C, pure compound)
Stability: Stable under ordinary environmental conditions. Decomposes slowly at melting point. Very slight hydrolytic decomposition at acid or neutral pH at ambient temperature. Strong sodium and potassium hydroxide solutions may cause spontaneous ignition of concentate forms. In neutral or weakly basic solution, captafol slowly decomposes at a rate depending upon pH and temperature, being very slow below 7.0 and rapid above 9.0.

Toxicity Characteristics:

Acute oral LD_{50} - Rat - males 6780 mg/kg, Category III
females 6330 mg/kg, Category III

Acute inhalation LC_{50} - Data gap

Dermal Irritation - Rabbit - moderate dermal irritation at 72 hours, Category III. Severe dermal sensitization.

Eye Irritation - Rabbit - corneal opacity, iris and conjunctive irritation present through day 21, Category I.

Teratology - Rat - no teratogenic effects seen. Highest dose tested: 100 mg/kg/day.
Rabbit - recently submitted tests currently under review.
Hamster - no effect level (NOEL) for fetotoxicity and possible teratogenic effects = 300 mg/kg. New study must be submitted by the registrant.

Oncogenicity - Mouse - Oncogenic lesions were observed at 1000 and 3000 parts per million (ppm) but not at 300 ppm. Information concerning the control groups is being requested from the registrant in order for a final risk assessment to be performed.
- Rat - Oncogenic lesions were seen at all dose levels. Additional histopathology examinations of liver and mammary tissues at low (56 ppm) and mid (241 ppm) dose levels have been requested from the registrant. This information is necessary for a complete risk assessment to be performed.

Physiological and Biochemical Behavioral Characteristics:

Foliar Absorption: Captafol and/or its metabolites and degradrates is (are) absorbed by roots and shoots of plants.

Translocation: Captafol and/or its metabolites and degradrates is (are) translocated in plant tissue. Captafol and/or its metabolites and degradates is (are) absorbed and translocated within plants as a result of seed treatment, soil treatment and foliar application.

Mechanism of Pesticidal Action: Unknown

Metabolism and Persistence in Plants and Animals: The metabolism and accumulation of captafol in plants are not understood. The metabolism of captafol is understood for ruminants but not for avian species.

The following metabolites have been identified in animal tissues:

delta^4-tetrahydrophthalimide

phthalimide

4,5-epoxyhexahydrophthalimide

4,5-dihydroxyhexahydrophthalimide

3-hydroxy-delta^4-tetrahydrophthalimide

5-hydroxy-delta^3-tetrahydrophthalimide

delta^4-tetrahydrophthalamic acid

delta^4-tetrahydrophthalic acid

The above metabolites, with the exception of delta^4-tetrahydrophthalic acid, were found in milk. No parent captafol per se was detected in ruminant tissues or in milk.

Environmental Characteristics:

Absorption and Leaching in Basic Soil Types:
Captafol per se does not leach from basic soils. The leachability and persistence of its metabolites and degradates are not understood.

Microbial Breakdown: Inadequate data. Limited data indicate that captafol per se has a half-life of <3, 5, and 8 days in nonsterile organic, sandy and clay loam soils, respectively. The soil degradates and metabolites have not been identified.

Loss from Photodecomposition and/or Volatilization: Inadequate data.

Bioaccumulation: No data.

Resultant Average Persistence: Inadequate data on metabolites and degradates.

Ecological Characteristics:

Hazards to fish and wildlife

Rainbow trout: 96-hr LC_{50} = 0.027 - 0.190 ppm
Bluegill sunfish: 96-hr LC_{50} = 0.045 - 0.230 ppm
Characterized as "very highly toxic" to both cold water and warm water fish. Inadequate data for fish accumulation.

Avian Toxicity: LD_{50} = >2510 ppm
LC_{50} = >5620 ppm

Daphnia magna: 96-hr LC_{50} = 3.34 ppm

Moderately to very highly toxic to freshwater invertebrates.

Avian Reproduction: Strong potential for reproductive effect in birds (based on supplementary information).

Potential problems related to endangered species:

Additional data on exposure persistence, avian reproduction studies, and accumulation are required to complete the endangered species assessment for captafol.

Efficacy Review Results:

Captafol product registrations with EPA have been supported with efficacy data. Tolerant strains of target plant pathogens have not been reported.

Tolerance Assessments:

1. List of Crops and Tolerances:

The following table lists the present status for tolerances in parts per million (ppm) for residues of captafol:

Raw Agricultural Commodity	Parts Per Million in Captafol Residues			
	U.S.	Canada	Mexico	Codex
Apples	0.25	0.1(N)	—	5.0
Apricots	30.0	0.5	—	15.0
Blueberries	35.0	—	—	—
Cherries, sour	50.0	10.0	—	10.0
Cherries, sweet	2.0	2.0	—	2.0
Citrus fruit	0.5	—	—	—
Corn, Fresh (sweet K+CWHR)	0.1 (N)	—	—	—
Cranberries	8.0	—	—	8.0
Cucumbers	2.0	2.0	—	2.0
Macadamia nuts	0.1(N)	—	—	0.1 (N)
Melons	5.0	2.0	—	2.0
Nectarines	2.0	—	—	—
Peanuts, hulls	2.0	—	—	—*
Peanuts, meats (hulls removed)	0.05	—	—	0.05
Onions	0.1(N)	0.1 (N)	—	0.5
Peaches	30.0	15.0	—	15.0
Pineapples	0.1(N)	—	—	10.0
Plums (fresh prunes)	2.0	0.2	—	10.0
Potatoes	0.5	0.1(N)	—	0.5
Taro (corms)	0.02	—	—	—
Tomatoes	15.0	5.0		5.0
Carrots				0.5

*Codex MRL for whole peanuts is 0.5 ppm.

2. Seed Applications:

No tolerances have been established for captafol in or on any crop for which captafol is registered solely for seed treatment or plant propagule uses, because heretofore seed treatment and plant propagule uses have been considered to be nonfood uses. These crops include: corn (field), cotton, rice, sorghum (grain and forage), strawberries (propagating bed use), and sugarcane (seed piece use).

Results of Tolerance Assessment:

Sufficient data are available to determine that the currently established tolerances for residue of captafol in or on the following commodities are adequate: apricots, blueberries, cranberries, macadamia nuts, nectarines, peaches, peanut hulls, and taro corms (40 CFR 180.267). However, additional data concerning residues of metabolite THPI must be submitted for all commodities since the residues of concern in or on plants have recently been modified to include THPI. In addition to THPI data, other residue data are required to support the tolerance for captafol in or on the following commodities: apples, citrus fruits, corn (sweet), cucumbers, melons, onions, peanuts, pineapples, plums (prunes), potatoes, and tomatoes. THPI data and tolerance changes must be submitted for sweet and sour cherries. Residue data and tolerance proposals must be submitted for the following commodities: crops receiving only seed treatments (cotton, field corn, rice and sorghum), pears (state label use only), strawberries [propagating bed use: Section 24(c)], sugarcane (seed piece use), and taro foliage. Tolerances for the following commodities are pending: carrots, coffee beans, pecans, soybeans, and soybean forage and hay. Plant metabolism of captafol is not adequately understood, therefore tolerance for residues other than captafol and THPI may need to be sought if those residues are deemed to be of concern. A poultry metabolism study will be needed. Also, feeding studies are required for ruminants and poultry. Additional storage stability data are necessary to validate the residue data. No crop group tolerance may be established based on the available data.

The Theoretical Maximum Residue Contribution (TMRC) is 1.4579 mg/day based on a 1.5-kg diet. The change in the residue definition (by including the metabolite THPI), the requested tolerance proposals and the pending tolerances noted above will affect a change in the TMRC level.

The maximum permissible intake (MPI) for a 60 kg person is 1.68 mg/day based on an acceptable daily intake (ADI) of 0.028 mg/kg. The present TMRC represents 86.8% of the MPI. The inclusion of the major metabolite (THPI) in the tolerance expression may result in an increase in the TMRC and a greater percentage of the MPI utilized.

The ADI for captafol is based on a chronic toxicity study in rats. A NOEL was established at 56 ppm for non-oncogenic effects. In that study the next highest dose level caused cholangiectasis in liver, increase in hyperplasia of tubule epithelium, megalocytic cells and transitional cell hyperplasia in kidney, increased erosion/ulceration, hyperkertosis/acanthosis, ground substance in glandular mucosa, and dilated pits in stomach. The reported dosage level was corrected from 75 ppm to 56 ppm based on the instability of captafol in the diet. In the rat, 56 ppm is approximately equivalent to 2.8 mg/kg. Using a safety factor of 100 and a NOEL of 2.8 mg/kg/day, the ADI would be 0.028 mg/kg for humans. The only registrant of technical captafol, Chevron Chemical Company, has been requested to complete the histopathology examination of the low and mid-dose liver and mammary gland tissues: therefore, the NOEL for cholangiectasis in the liver may change. The NOEL of 56 ppm is for systemic effects excluding the issue of oncogenicity for which a risk assessment will be performed.

Problems that are Known to Have Occurred with Use of the Chemical

1. Captafol is a skin sensitizer. Incidents of farmworkers being disabled from its effect have been reported. Restricting the use of captafol to mechanically harvested tomatoes, and labeling requiring use of gloves and protective clothing by citrus harvesters have reduced this problem.

4. Summary of Regulatory Positions and Rationale

Based on the oncogenic and fish toxicity potential risks of hazard, captafol is being placed under Special Review by the Environmental Protection Agency. The presumption of risk of hazards outweighing the derived benefits must be rebutted by the manufacturers of pesticide products that have captafol as an active ingredient. Based on the oncogenic potential and the fish toxicity potential, captafol is classified as a "Restricted Use" pesticide. All captafol products must be relabeled as "Restricted Use" pesticides.

The following labeling restrictions will be required for continued registration of captafol products:

All technical grade, manufacturing-use (MUP's) and end-use products (EUP's) must bear appropriate labeling as specified below and in 40 CFR 162.10.

1. Precautionary statements to be used on labeling of all end-use captafol products:

   a. All end-use product labels must reflect the following statements:
   RESTRICTED USE PESTICIDE. For retail sale to, and use only by Certified Applicators or persons under the direct supervision of a Certified Applicator, and only for those uses covered by the Certified Applicator's certification.
   "This product is classified as a "Restricted Use Pesticide" because it contains captafol which has been determined to cause tumors in laboratory animals."

   Exposure to captafol during mixing, loading, and application may be hazardous to your health.
   This product contains captafol which has been determined to cause tumors in laboratory animals.

   b. All end-use products must have the labeling precaution under "Direction for Use": Wear impervious gloves and full body clothing during handling and application".

c. All end-use products intended for crop use, except seed, seed piece, and plant propagule treatments must bear the following use restrictions:

i. Do not rotate treated crop with crops other than those with registered captafol uses.

ii. Do not allow persons to enter treated areas within 24 hours following application unless full body clothing is worn. Conspicuously post reentry information at sites of application.

iii. Do not use captafol-treated rice seed in fields subsequently to be used for agricultural crops other than those with registered captafol uses

iiii. Water from cranberry bogs, wetland taro fields (foliarly treated with captafol) and rice fields planted with captafol-treated rice seed must not be used for irrigation of crops other than those with registered captafol uses.

2. For products that bear label claims for use in greenhouses:

a. Only the applicator is permitted in the greenhouse during application of captafol to soil. Open vents to greenhouse during application and for at least 1 hour after application.

b. Workers planting in captafol treated soil in greenhouses must wear impervious gloves and full body clothing.

3. All products, manufacturing-use and end-use, must bear the labeling precautionary statements.

DANGER

Causes irreversible eye damage. Harmful if swallowed or inhaled. May cause allergic skin reactions. Do not get in eyes. Wear goggles or face shield when handling. Avoid contact with skin and clothing. Remove and separately launder clothing before reuse.
This product contains captafol which has been determined to cause tumors in laboratory animals

In addition, the following specific environmental hazard labeling requirements apply to either technical, manufacturing-use or end-use product as indicated.

a. All technical and MUP's must bear the following precautionary statements:

> This pesticide is extremely toxic to fish. Do not discharge into lakes, streams, ponds, or public waters unless in accordance with an NPDES permit. For guidance contact your Regional Office of the Environmental Protection Agency. Do not discharge effluent containing captafol into sewage systems without obtaining permission from the sewage treatment authority.

b. All EUP's that allow for foliar applications except foliar application to cranberries, must bear the hazard precaution:

> This pesticide is extremely toxic to fish. Do not apply directly to water. Drift and runoff from treated areas may be hazardous to aquatic organisms in neighboring areas. Do not contaminate water by cleaning of equipment or disposal of wastes.

c. All EUP's that allow foliar application to cranberries must bear the following environmental hazard precautions:

> This pesticide is extremely toxic to fish. Fish may be killed at recommended application rates. Drift and runoff from treated areas may be hazardous to aquatic organisms in neighboring areas. Do not contaminate water by cleaning of equipment or disposal of wastes.

d. All EUP's that allow seed treatment must bear the following environmental hazard precaution:

> This pesticide is extremely toxic to fish. Do not contaminate water by cleaning of equipment or diposal of wastes.

4. Both MUP's and EUP's may need special labeling to protect endangered species. This will be determined after required environmental chemistry data are reviewed, and in conjunction with EPA's evaluation of the potential risk of hazards to endangered species.

Based on historical use experience (human health effects reports) and the benefits from the pesticide uses, the Agency will allow the registration of captafol products to continue for existing use-patterns until the risk of hazards is better defined by the data submitted in response to the Captafol Registration Standard and the completion of a Special Review by the Agency; and provided that the required labeling under the Standard is submitted within the time specified.

5. Summary of Major Data Gaps

Product Chemistry Data (6)[a]
- Description of beginning materials and manufacturing process
- Discussion of Formation of Impurities
- Preliminary Analysis of Product Samples
- Density, Bulk Density, or Specific Gravity
- Vapor Pressure
- Dissociation Constant
- Octanol/Water Partition Coefficient
- pF
- Solubility

Toxicology
- Inhalation LC_{50} - Rat (6)
- 90-day feeding - Rodent, Non-rodent (18)
- 90-day Inhalation - Rat (18)
- Chronic Toxicity - 2 species: Rodent and Non-rodent (36)
- Oncogenicity study - 2 species: Rat and Mouse preferred (6)
- Teratogenicity 2 species - needs hamsters study using two test groups, one dosed on day 7, and the other dose on day 8 of gestation (12)
- Gene Mutation (12)
- Dermal Absorption (6)

Residue Chemistry (24)
- Analytical Method
- Plant Metabolism
- Animal Metabolism (poultry)
- Storage Stability
- Magnitude of Residues on all food-use crops

Environmental Fate
- Soil Metabolism - Aerobic soil (24)
  - Anaerobic aquatic (24)
  - Aerobic aquatic (24)
- Degradation - Hydrolysis (6)
  - Photodegradation in water, soil and air (6)
- Dissipation - Soil (24)
  - Aquatic (sediment) (24)
- Reentry (24)

a/ Data to be submitted in number of months after receipt of the Guidance for the Reregistration of Pesticide Products Containing Captafol, EPA Case Number 116.

Mobility Studies (6)[a]
Leaching and Absorption/Desorption
Accumulation Studies (24)
Rotational Crops
Wildlife and Aquatic Organisms
Acute LC_{50} Estuarine and
Marine Organisms (6)

6. Contact Person

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a. Data to be submitted in number of months after receipt of the Guidance for the Reregistration of Pesticide Products Containing Captafol, EPA Case Number 116.